

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
30 November 2000 (30.11.2000)

PCT

(10) International Publication Number  
**WO 00/71571 A3**

(51) International Patent Classification<sup>7</sup>: **C07K 1/107**,  
1/06, 5/11, 5/117, 5/062, 9/00, A61K 38/04, A61P 35/00

(21) International Application Number: PCT/EP00/04261

(22) International Filing Date: 11 May 2000 (11.05.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/134,136 14 May 1999 (14.05.1999) US

(71) Applicant (for all designated States except US):  
**BOEHRINGER INGELHEIM** [DE/DE]; Pharma  
KG, D-55216 Ingelheim am Rhein (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **PARK, John**,  
**Edward** [US/DE]; Widdersteinstrasse 162, D-88400  
Biberach/Riss (DE). **RETTIG, Wolfgang, J.** [DE/DE];  
Magnolienweg 7, D-88400 Biberach/Riss (DE). **LENTER**,  
**Martin** [DE/DE]; Promenade 23, D-89073 Ulm (DE).  
**PETERS, Stefan** [DE/DE]; Ringgasse 25, D-55218 In-  
gelheim am Rhein (DE). **MACK, Jürgen** [DE/DE]; Am-  
riswilstrasse 7, D-88400 Biberach/Riss (DE). **LEIPERT**,  
**Dietmar** [DE/DE]; Albrecht-Dürer-Strasse 17, D-55218

Ingelheim am Rhein (DE). **GARIN-CHESA, Pilar**  
[ES/DE]; Magnolienweg 7, D-88400 Biberach/Riss (DE).  
**FIRESTONE, Raymond, Armand** [US/US]; 59 Barnes  
Road, Stamford, CT 06902 (US). **TELAN, Leila, A.**  
[US/US]; 14 Evergreen Square, Apt.3, Somerville, MA  
02143 (US).

(74) Agent: **LAUDIEN, Dieter**; Boehringer Ingelheim GmbH,  
D-55216 Ingelheim am Rhein (DE).

(81) Designated States (*national*): AE, AU, BG, BR, CA, CN,  
CZ, EE, HU, ID, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL,  
RO, SG, SI, SK, TR, UA, US, UZ, VN, YU, ZA.

(84) Designated States (*regional*): Eurasian patent (AM, AZ,  
BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE,  
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,  
NL, PT, SE).

Published:

— with international search report

(88) Date of publication of the international search report:  
7 September 2001

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

WO 00/71571 A3

(54) Title: FAP-ACTIVATED ANTI-TUMOR COMPOUNDS

(57) Abstract: The invention relates to a prodrug that is capable of being converted into a drug by the catalytic action of human fibroblast activation protein (FAP $\alpha$ ), said prodrug having a cleavage site which is recognised by FAP $\alpha$ , and said drug being cytotoxic or cytostatic under physiological conditions.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/04261

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K1/107 C07K1/06 C07K5/11 C07K5/117 C07K5/062  
C07K9/00 A61K38/04 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	PARK, JOHN E. ET AL.: "FIBROBLAST ACTIVATION PROTEIN A DUAL SPECIFICITY SERINE PROTEASE EXPRESSED IN REACTIVE HUMAN TUMOR STROMAL FIBROBLASTS" J BIOL CHEM (1999) 274(51) 36505-36512, XP002163938 the whole document	1-30
X	WO 97 12624 A (DEFEO JONES DEBORAH ;FENG DONG MEI (US); OLIFF ALLEN I (US); GARSK) 10 April 1997 (1997-04-10) cited in the application abstract; claims	1-30

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*G\* document member of the same patent family

Date of the actual completion of the international search

27 March 2001

Date of mailing of the international search report

09/04/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Cervigni, S

# INTERNATIONAL SEARCH REPORT

In. ational Application No

PCT/EP 00/04261

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 14416 A (DEFEO JONES DEBORAH ; SCOLNICK EDWARD M (US); OLIFF ALLEN I (US); G) 24 April 1997 (1997-04-24) cited in the application abstract; claims ---	1-30
X	WO 97 45117 A (PROTOTEK INC ; SMITH ROBERT E (US)) 4 December 1997 (1997-12-04) abstract; claims ---	1-10, 13-19
X	EP 0 255 341 A (SUNSTAR KK) 3 February 1988 (1988-02-03) abstract; example 7 ---	1-10
X	EP 0 126 685 A (CENTRE NAT RECH SCIENT) 28 November 1984 (1984-11-28) page 4, line 20 - line 22 page 7 page 5; claims ---	1-21, 28-30
X	CALICETI P ET AL: "PREPARATION AND PROPERTIES OF MONOMETHOXY POLY(ETHYLENE GLYCOL) DOXORUBICIN CONJUGATES LINKED BY AN AMINO ACID OR A PEPTIDE AS SPACER" FARMACO, SOCIETA CHIMICA ITALIANA, PAVIA, IT, vol. 48, no. 7, 1 July 1993 (1993-07-01), pages 919-932, XP000371926 ISSN: 0014-827X page 921 ---	21
X	WO 98 04277 A (UNIV PITTSBURGH) 5 February 1998 (1998-02-05) the whole document ---	21
X	DE 196 40 970 A (BAYER AG) 16 April 1998 (1998-04-16) the whole document ---	21
X	WO 98 13059 A (SQUIBB BRISTOL MYERS CO) 2 April 1998 (1998-04-02) the whole document ---	22-27
X	EP 0 624 377 A (SQUIBB BRISTOL MYERS CO) 17 November 1994 (1994-11-17) the whole document -----	22-27

# INTERNATIONAL SEARCH REPORT

Information on patent family members

In International Application No

PCT/EP 00/04261

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9712624 A	10-04-1997	US 5866679 A AU 7203496 A CA 2233272 A EP 0853483 A JP 10512588 T US 6130204 A	02-02-1999 28-04-1997 10-04-1997 22-07-1998 02-12-1998 10-10-2000
WO 9714416 A	24-04-1997	AU 708475 B AU 7432196 A EP 0855910 A JP 2000506494 T	05-08-1999 07-05-1997 05-08-1998 30-05-2000
WO 9745117 A	04-12-1997	AU 3224997 A CZ 9803893 A EP 0914123 A	05-01-1998 14-07-1999 12-05-1999
EP 0255341 A	03-02-1988	JP 2516365 B JP 63277966 A JP 1923995 C JP 6048998 B JP 63036800 A JP 1888076 C JP 6011240 B JP 63087999 A AT 85362 T CA 1310893 A DE 3783966 A DE 3783966 T ES 2053547 T GR 3006962 T US 5137811 A	24-07-1996 15-11-1988 25-04-1995 29-06-1994 17-02-1988 22-11-1994 16-02-1994 19-04-1988 15-02-1993 01-12-1992 18-03-1993 27-05-1993 01-08-1994 30-06-1993 11-08-1992
EP 0126685 A	28-11-1984	FR 2546163 A JP 60004158 A US 4703107 A	23-11-1984 10-01-1985 27-10-1987
WO 9804277 A	05-02-1998	US 5952294 A AU 3652797 A CA 2261886 A EP 0918534 A	14-09-1999 20-02-1998 05-02-1998 02-06-1999
DE 19640970 A	16-04-1998	AU 4776697 A WO 9815571 A EP 0929570 A JP 2001502308 T	05-05-1998 16-04-1998 21-07-1999 20-02-2001
WO 9813059 A	02-04-1998	AU 4599597 A EP 0961619 A	17-04-1998 08-12-1999
EP 0624377 A	17-11-1994	AU 687795 B AU 6302694 A CA 2123363 A CN 1100426 A CZ 9401187 A FI 942237 A HU 66485 A JP 7070175 A MX 9403570 A	05-03-1998 17-11-1994 15-11-1994 22-03-1995 16-11-1994 15-11-1994 28-11-1994 14-03-1995 31-01-1995

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 00/04261

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0624377 A		NO 941819 A	15-11-1994
		NZ 260512 A	25-09-1996
<hr/>			